REMARKS

Claims 1-5, 8, 10 and 28-40 are pending. Applicants have herein amended claims 1, 2, 8, and 31. Support for these amendments may be found in the original claims and in the specifications, inter alia, as follows: page 2, lines 6 to 9; page 3, first paragraph; page 4, lines 3 to 5; page 8, lines 16-18; page 10, lines 1 to 5 and lines 23-28; page 13, line 25 to page 14, line 16; page 30, lines 24 to 32; Examples 9.1, 9.2, and 9.3 at pages 47 through page 52 line 13; and the original claims 8-10

Rejections under 35 U.S.C. §112, first paragraph – scope of enablement

The Examiner rejected all pending claims, alleging that the specification, while enabling for method for identifying binding analogs which interact with the claimed fragments of SEQ ID NOs: 4, 6, and 8, is not enabling for the full scope of the claims. Specifically, the Examiner maintained the previous rejections of claims 1-5 and 8-10 as not enabled for methods of identifying binding analogs of proteins which are at least 40% identical to residues 23-132 of SEQ ID NO:8, or any polypeptide chain which is encoded by nucleic acids amplified by the primers of SEQ ID NO: 12-15, or which hybridizes to residues 256-552 of SEQ ID NO:8. The Examiner also rejected claims 28-40 for the same reasons.

In response to the Examiner's rejection, Applicants have amended the claims to remove the recitation of binding analogs with 40% identity with residues 23-132 of SEQ ID NO: 8; and the recitation of polypeptide encoded by nucleic acids amplified by primers of SEQ ID NO: 12-15. Applicants also amended the claims to more specifically recite the hybridization condition for nucleic acids that hybridize to residues 256-552 of SEQ ID NO:8. The hybridization condition now recited in the claims can be found in the specification at page 8, lines 16-18, and enables one to practice the claimed invention. Applicants believe the amendment addresses the Examiner's concern and respectfully request that the rejection on this ground be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph – new matter

The Examiner rejected all pending claims as introducing new matter. Applicants respectfully traverse. All claims have support in the specifications and, for dependent claims, in the claims from which they depend, as indicated below.

Claim 1 recites a binding analog "for a receptor of a morphogen, said morphogen being characterized as sharing at least 60% amino acid sequence identity or 70 % amino acid sequence homology to the sequence of C-terminal 102 amino acids of SEQ ID NO:7, and being able to substitute for OP-1 in binding to SEQ ID NOs 4,6, or 8" as a result of last amendment. The support for the recitation can be found at page 10, lines 23-28.

Claim 2 contains a recitation "wherein detection of induction of said OP-1 mediated cellular response is indicative that said candidate analog is an OP-1 receptor-binding analog," as a result of last amendment. The support for this amendment can be found in the original claim and the specification, at page 2, lines 6 to 9; page 3, first paragraph; page 4, lines 3 to 5; page 10, lines 1 to 5; page 30, lines 24 to 32; and Examples 9.1, 9.2, and 9.3 at pages 47 through page 52 line 13.

Claim 3 is dependent on claim 2, and no new language has been introduced in claim 3 itself. Claims 4 and 5 are dependent on claims 2 or 3. The support for these claims can be found in claims 2 and/or 3, which in turn are supported by the specification as described above. Claim 4 additionally contains a recitation "wherein the activity of said reporter gene can be detected as said OP-1-mediated cellular response upon stimulation by OP-1 analog thereof in said cells." The support for this amendment can be found in the same sections of the specification as for the amendment of claim 2, particularly Example 9.2 at page 50, line 17 to page 51, line 9.

Claim 8 contains a recitation "means for detecting induction of an OP-1-mediated cellular response as a means for detecting interaction of OP-1 or candidate OP-1 receptor-binding analog with said protein of part (a)" as a result of last amendment. The support for this recitation can be found in the same portion of the specification as the support for claim 2. Claim 10 is dependent on claim 8, and no new language has been introduced to claim 10 itself.

Claims 28, 29 and 32-34 are dependent on claim 1 and claims 35-37 are dependent on claim 2. The support for these claims are found in claims 1 and 2, respectively.

Claim 31 claims a kit which contains components to practice the method of claim 1. The support for claiming kits is found in the original claims 8-10, and in the specification at page 13,

line 25 to page 14, line 16. The support for the recited morphogen can be found in the specification in the same sections as the support for the amendment to claim 1.

Claims 38-40 are dependent on claims 8 or 31. The support for these claims can be found in claims 8 and 31.

Accordingly, Applicants submit that all claims and their amendments are supported by the specification and the original claims, and there is no new matter introduced. Applicants believe the above remarks address the Examiner's concern and respectfully request that the rejection on this ground be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph – written description

All pending claims were rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of the application, had possession of the claimed invention.

In response to the Examiner's rejection, Applicants have amended the claims to remove the recitation of binding analogs with 40% identity with residues 23-132 of SEQ ID NO: 8; and the recitation of polypeptide encoded by nucleic acids amplified by primers of SEQ ID NO: 12-15. Applicants also amended the claims to more specifically recite the hybridization condition for nucleic acids that hybridize to residues 256-552 of SEQ ID NO:8. The hybridization condition now recited in the claims is supported by the specification at page 8, lines 16-18.

The Examiner stated that the conditions described in the instant specification is not as stringent as the stringency condition in Example 9 of the "Revised Interim Written Description Guidelines Training Materials" (the "Guideline") published on the U.S.P.T.O. web site. Applicants point out that notably the Examiner did not state, but more importantly, the Guideline does not state, that the high stringency condition of Example 9 is *necessary* for written description of nucleic acid defined by hybridization. Applicants submit that although the conditions set forth in the Guideline are sufficient, they are not necessary.

Applicants submit that the conditions disclosed in the instant specification are expected to yield nucleic acids that one skilled in the art regards as sufficiently related to each other and

therefore provide sufficient structural information of such nucleic acids to satisfy the written description requirement. Applicants have amended the claims to recite a specific hybridization condition. In a widely accepted textbook of molecular biology "Molecular Cloning," (Sambrook *et al.*, eds., 1989, Cold Spring Harbor Press, Cold Spring Harbor, NY) the following statement can be found on page 9.50 paragraph "9." : "In general, washing conditions should be as stringent as possible (*i.e.*, a combination of temperature and salt concentration should be chosen that is approximately 12-20°C below the calculated Tm of the hybrid under study)." The reference also gives an equation that can be used to estimate the Tm for a given hybrid:

$$Tm=81.5°C + 16.6(\log_{10}[Na+]) + 0.41(\text{fraction G+C}) - 0.63(\%\ \text{formamide})-(600/l)$$

where l is the length of the hybrid in base pairs. The washing solution of the method in the instant application has [Na+] of 0.0195M (0.016M from 0.1 X SSPE, 0.0035M from 0.1% SDS), fraction G+C is 48% (84 As, 70 Ts, 79 Cs, 64 Gs), % formamide is 0, and l is 297, which, according to the equation, results in the Tm of approximately 70°C. The washing temperature of the method in the instant application is 50°C, which is about 20°C below the Tm, falling within the range that Sambrook considered stringent and to yield nucleic acids with sequences specifically related to the original sequence. Accordingly, Applicants submit that the amended claims reciting a hybridization condition adequately describe the structural and functional characteristics of the nucleic acids to practice the claimed method and therefore satisfy the written description requirement.

Applicants respectfully request that the rejection on this ground be withdrawn in view of the amendment and above remarks.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 1, 2, and 8, alleging that the recited term "stringent conditions" of hybridization is vague and indefinite. Applicants have amended claims 1, 2 and 8 to recite a set of hybridization conditions, in accord with the Examiner's suggestion in the office action. Applicants submit that the amendment obviates the Examiner's rejection.

Double patenting

The Examiner maintained the provisional rejection under the judicially created doctrine of double patenting over one or more claims of copending Application No. 09/267,963. This application issued as U.S. Patent No. 6,692,925 (the "'925 patent") on February 17, 2004. Upon reviewing the issued claims, Applicants submit that this is an improper double patenting rejection.

In the office action, the Examiner provides his basis for the obviousness rejection as "application being drawn to proteins having serine/threonine kindase domains." The claims of the '925 patent are all directed to methods "for determining if a substance inhibits TGF-β/Alk1 induced Smad1 phosphorylation." The claims of the instant application do not recite TGF-β, Alk1, Smad1, nor Smad1 phosphorylation. Applicants' claims relate to, among other things, identifying morphogen receptor biding analogs. Conversely, the claims of the '925 patent are not directed to such. Nothing in the claims of the '925 patent makes the claims of the instant application obvious. Accordingly, Applicants request that the Examiner reconsider and withdraw this ground of rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

The requisite fee for a two-month extension of time should be charged to our Deposit Account No. 18-1945, under Order No. JJJ-P04-523. Applicant believes additional no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P04-523 from which the undersigned is authorized to draw.

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Respectfully submitted,

By_____

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